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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,113	03/24/2004	Keith R. Hildebrand	P-20907.00US	4515

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MEDTRONIC, INC.
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EXAMINER	
STITZEL, DAVID PAUL	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/808,113	HILDEBRAND ET AL.	
	Examiner	Art Unit	
	David P. Stitzel, Esq.	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☒ Claim(s) *29 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

OFFICIAL ACTION

Status of Claims

Claims 1-38 are currently pending and therefore examined herein on the merits for patentability.

Claim Objections

Claims 29-30 are objected to because of the following informalities: "gababentin" should be rewritten as "gabapentin." Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-7 and 26-31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of the Carter '881 publication in view of U.S. Patent 4,024,175 (hereinafter the Satzinger '175 patent).

With respect to claims 1-7 of the instant application, the Carter '881 publication teaches a process for preparing an injectable pharmaceutical composition for use in the treatment of epilepsy, said injectable pharmaceutical composition may comprise gabapentin in combination with a physiologically acceptable carrier or excipient, wherein said process includes sterilizing said composition by filtering; sterilizing said composition by heating with an autoclave; aseptically filling

an ampoule with said composition; and sterilizing said ampoule containing said composition (page 8, lines 1-2; page 9, lines 26-28; page 10, lines 3, 25-27 and 31; page 11, lines 7-18 and 28-32; page 12, lines 1-7; page 28, lines 1-11). Although said injectable pharmaceutical composition *may* comprise gabapentin (page 9, lines 26-28; and page 10, line 3), it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to in fact utilize gabapentin as the Carter '881 publication teaches that the compounds of the invention are useful in the treatment of epilepsy (page 8, lines 1-2), as is gabapentin. Therefore, one of ordinary skill in the art would have been motivated to utilize gabapentin, in combination with the compounds of the invention taught in the Carter '881 publication, so as to obtain an injectable pharmaceutical composition for use in the treatment of epilepsy, wherein said injectable pharmaceutical composition comprises not one, but two compounds possessing anti-epileptic properties.

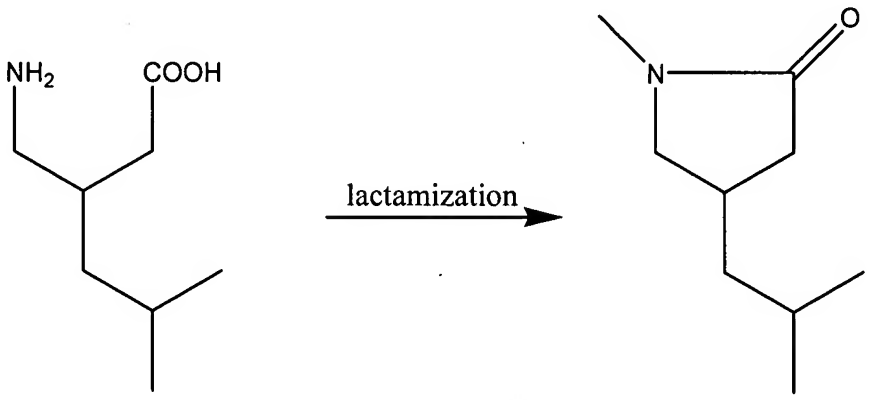
With respect to claims 1-7 and 26-31 of the instant application, although the Carter '881 publication discloses a process for preparing an injectable pharmaceutical composition, which may comprise gabapentin, for use in the treatment of epilepsy, as discussed hereinabove, the Carter '881 publication does not teach an injectable dosage amount of said gabapentin. However, the Satzinger '175 patent teaches an injectable pharmaceutical composition for use in the treatment of epilepsy, said injectable pharmaceutical composition comprising: gabapentin; and a pharmacologically compatible carrier or diluent, wherein said gabapentin is parenterally administered in an injectable dosage amount ranging from 5 mg to 50 mg (column 1, lines 5-12 and 26-29; and column 3, lines 24-52). As a result, the Satzinger '175 patent teaches parenterally administering gabapentin in an injectable dosage amount ranging from 5 mg to 50 mg so as to impart anti-epileptic properties to said injectable pharmaceutical composition. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at

the time the instant application was filed to prepare the injectable pharmaceutical composition, as taught by the Carter '881 publication, having an injectable dosage amount of gabapentin ranging from 5 mg to 50 mg for parenteral administration so as to impart desired anti-epileptic properties to said injectable pharmaceutical composition. In addition however, while the Satzinger '175 patent does not explicitly teach the instantly claimed concentrations (i.e., specific weight per volume) of gabapentin present within said the injectable pharmaceutical composition, it is well within the purview of the skilled artesian to determine the desired optimal workable concentrations of gabapentin by systematically adjusting the injectable dosage amounts of gabapentin, as taught in the Satzinger '175 patent, within a given per unit volume during the course of routine experimentation. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

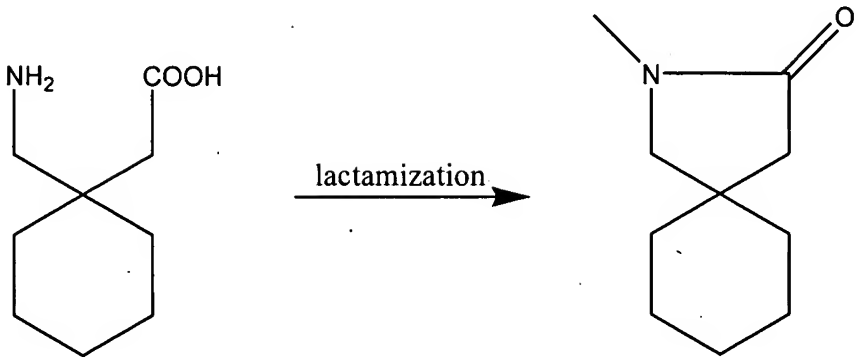
2. Claims 8-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Carter '881 publication in view of the Satzinger '175 patent, and in further view of U.S. Patent 5,603,894 (hereinafter the Aikus '894 patent) and in further view of U.S. Patent 6,046,353 (hereinafter the Grote '353 patent).

The teachings of the Carter '881 publication and the Satzinger '175 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

With respect to claims 8-20 of the instant application, while neither the Carter '881 publication, nor the Satzinger '175 patent teach heat sterilization at either a specific temperature (i.e., between about 105°C and about 140°C) for a specific duration in time (i.e., between about 2 minutes and about 60 minutes), or a specific degree of sterilization F_0 (i.e., F_0 of about 1 to 24 or greater), the Aikus '894 patent teaches a method of sterilizing a pharmaceutical composition comprising a heat sensitive compound by heating said composition to an elevated temperature for a short period of time, wherein the temperature and the time required to obtain a desired degree of sterilization F_0 (*generally* greater than 6, and preferably greater than 8, at an elevated temperature of about 121°C) are calculated and adjusted so as to minimize thermal degradation of said heat sensitive compound (column 1, lines 6-13; column 2, lines 47-53; and column 4, lines 27-45). In addition, the Grote '353 patent teaches limiting the duration of heat exposure of a heat sensitive compound, namely 3-(aminomethyl)-5-methylhexanoic acid (which is structurally similar to gabapentin), so as to minimize undesired decomposition and lactamization of 3-(aminomethyl)-5-methylhexanoic acid to the corresponding lactam (column 14, lines 41-48; column 15, lines 56-67; and column 16, lines 1-9), as illustrated hereinbelow:



3-(aminomethyl)-5-methylhexanoic acid corresponding lactam



gabapentin (i.e., 2-(1-(aminomethyl)cyclohexyl)acetic acid) gabapentin lactam

Furthermore, while none of the aforementioned references explicitly teach each of the instantly claimed elevated temperatures, durations of time and degrees of sterilization F_0, it is well within the purview of the skilled artesian to determine the desired optimal workable elevated temperatures, durations of time and degrees of sterilization F_0, by systematically adjusting the aforementioned parameters during the course of routine experimentation so as to obtain a desired degree of sterilization F_0, while minimizing the degree of thermal degradation of said heat sensitive composition due to extended durations of exposure to elevated temperatures. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003). Sufficient motivation, as well as a reasonable expectation of success, exists to combine the aforementioned references, as they collectively teach heat sterilizing a heat sensitive compound by limiting the duration of heat exposure of said heat sensitive

compound, so as to obtain a desired degree of heat sterilization while minimizing undesired thermal degradation of said heat sensitive compound.

3. Claims 21-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Carter '881 publication in view of the Satzinger '175 patent, and in further view of U.S. Patent 6,054,482 (hereinafter the Augart '482 patent).

The teachings of the Carter '881 publication and the Satzinger '175 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

With respect to claims 21-25 of the instant application, while neither the Carter '881 publication, nor the Satzinger '175 patent teach a specific weight per volume percentage of the corresponding undesirable lactam within said composition, the Augart '482 patent teaches a pharmaceutical composition for use in the treatment of epilepsy, said composition comprising gabapentin, wherein the specific weight percent of the corresponding undesirable lactam within said composition is less than or equal to 0.5% by weight (abstract; column 1, lines 10-21; column 2, lines 16-52; column 3, lines 26-35; column 4, lines 50-53; column 5, lines 5-67; and column 6, lines 1-5). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to modify both the Carter '881 publication and the Satzinger '175 patent, with the teachings of the Augart '482 patent, so as to provide a pharmaceutical composition comprising gabapentin for use in the treatment of epilepsy, wherein said composition has a weight percent of the corresponding undesirable lactam of less than or equal to 0.5% by weight. One of ordinary skill in the art would have been motivated to decrease the concentration of the corresponding undesirable lactam so as to thereby decrease the level of toxicity within said composition, said toxicity being associated

with and attributable to the amount of corresponding undesirable lactam present with said composition, as taught by the Augart '482 patent (column 4, lines 50-53).

4. Claims 21-25 and 32-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Carter '881 publication in view of the Satzinger '175 patent, and in further view of U.S. Pre-Grant Patent Application Publication Number 2002/0198261 (hereinafter the Kulkarni '261 publication).

The teachings of the Carter '881 publication and the Satzinger '175 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

With respect to claims 21-25 of the instant application, while neither the Carter '881 publication, nor the Satzinger '175 patent teach a specific weight per volume percentage of the corresponding undesirable lactam within said composition, the Kulkarni '261 publication teaches a pharmaceutical composition for use in the treatment of epilepsy, said composition comprising gabapentin, wherein the specific weight percent of the corresponding undesirable lactam within said composition is less than or equal to 0.5% by weight (abstract; [0001]-[0007]; [0009]-[0015]; [0068]; [0071]-[0072]; [0074]; [0077]; [0080]-[0085]; and claim 14). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to modify both the Carter '881 publication and the Satzinger '175 patent, with the teachings of the Kulkarni '261 publication, so as to provide a pharmaceutical composition comprising gabapentin for use in the treatment of epilepsy, wherein said composition has a weight percent of the corresponding undesirable lactam of less than or equal to 0.5% by weight. One of ordinary skill in the art would have been motivated to decrease the concentration of the corresponding undesirable lactam so as to thereby decrease the level of toxicity within said composition, said toxicity being associated with and attributable to the amount of

corresponding undesirable lactam present with said composition, as taught by the Kulkarni '261 publication [0010] and [0077].

With respect to claims 32-34 of the instant application, while neither the Carter '881 publication, nor the Satzinger '175 patent teach utilizing sodium hydroxide and hydrochloric acid as pH buffers, in the absence of preservatives, the Kulkarni '261 publication teaches a pharmaceutical composition for use in the treatment of epilepsy, said composition comprising gabapentin, sodium hydroxide and hydrochloric acid, in the absence of preservatives (abstract; [0001]-[0007]; [0009]-[0015]; [0068]; [0071]-[0072]; [0074]; [0077]; [0080]-[0085]; and claim 14). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to modify both the Carter '881 publication and the Satzinger '175 patent, with the teachings of the Kulkarni '261 publication, so as to provide a pharmaceutical composition for use in the treatment of epilepsy, wherein said composition comprises gabapentin, sodium hydroxide and hydrochloric acid, in the absence of preservatives. One of ordinary skill in the art would have been motivated to utilize sodium hydroxide and hydrochloric acid as pH buffers, in the absence of preservatives (as the addition of preservatives is not necessary [0074]), within said composition, so as to buffer said composition to a pH of about 5.5 to about 7.0 so as to substantially avoid undesired lactam formation, as taught by the Kulkarni '261 publication [0071]-[0072].

With respect to claim 35 of the instant application, although the Carter '881 publication teaches a process for sterilizing an injectable pharmaceutical composition by filtering, the Carter '881 publication does not specifically mention a particular pore size of about 0.22 μm. However, while the Carter '881 publication does not explicitly teach the instantly claimed filtration pore size it is well within the purview of the skilled artesian to determine the optimal filtration pore size by systematically

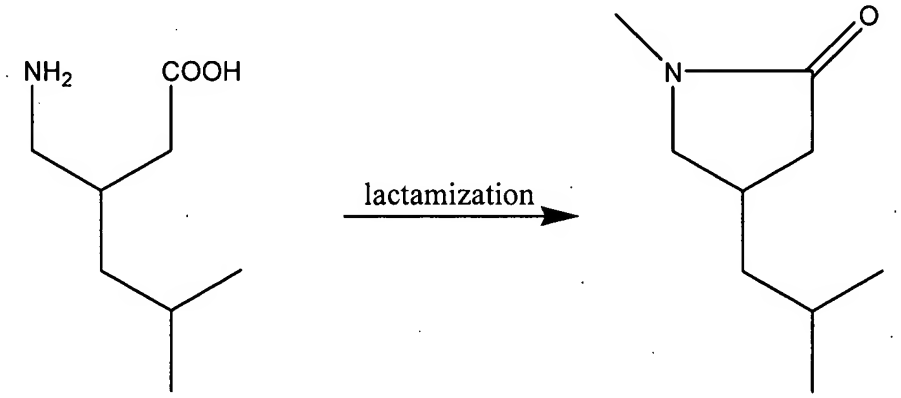
adjusting the concentrations thereof during the course of routine experimentation. One of ordinary skill in the art at the time the instant application was filed would have been motivated to systematically adjust the filtration pore size during the course of routine experimentation to obtain a desired specific degree of sterilization F_0. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

5. Claims 36-38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Carter '881 publication in view of the Satzinger '175 patent, in further view of the Kulkarni '261 publication as applied to claim 33 above, and in further view of the Aikus '894 patent and the Grote '353 patent.

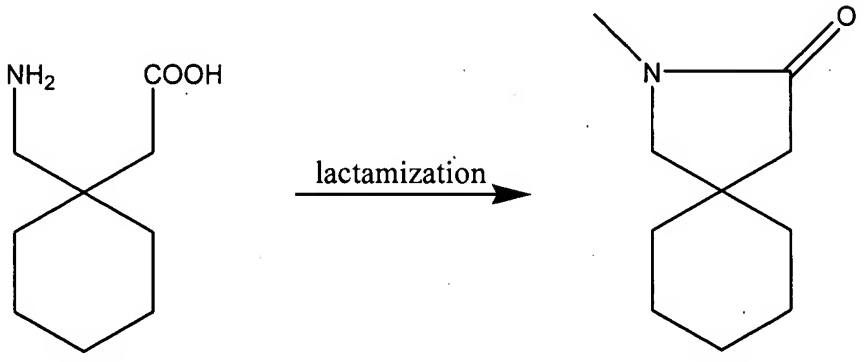
The teachings of the Carter '881 publication in view of the Satzinger '175 patent, in further view of the Kulkarni '261 publication as applied to claim 33 are therefore applied in the instant rejection as discussed hereinabove.

While neither the Carter '881 publication, the Satzinger '175 patent, nor the Kulkarni '261 publication explicitly teach heat sterilization at either a specific temperature (i.e., between about 105°C and about 140°C) for a specific duration in time (i.e., between about 2 minutes and about 60 minutes), or a specific degree of sterilization F_0 (i.e., F_0 of about 1 to 24 or greater), the Aikus '894 patent teaches a method of sterilizing a pharmaceutical composition comprising a heat sensitive compound by heating said composition to an elevated temperature for a short period of time, wherein the temperature

and the time required to obtain a desired degree of sterilization F_0 (*generally* greater than 6, and preferably greater than 8, at an elevated temperature of about 121°C) are calculated and adjusted so as to minimize thermal degradation of said heat sensitive compound (column 1, lines 6-13; column 2, lines 47-53; and column 4, lines 27-45). In addition, the Grote '353 patent teaches limiting the duration of heat exposure of a heat sensitive compound, namely 3-(aminomethyl)-5-methylhexanoic acid (which is structurally similar to gabapentin), so as to minimize undesired decomposition and lactamization of 3-(aminomethyl)-5-methylhexanoic acid to the corresponding lactam (column 14, lines 41-48; column 15, lines 56-67; and column 16, lines 1-9), as illustrated hereinbelow:



3-(aminomethyl)-5-methylhexanoic acid corresponding lactam



gabapentin (i.e., 2-(1-(aminomethyl)cyclohexyl)acetic acid) gabapentin lactam

Therefore, while none of the aforementioned references explicitly teach each of the instantly claimed elevated temperatures, durations of time and degrees of sterilization F_0, it is well within the purview of the skilled artesian to determine the desired optimal workable elevated temperatures, durations of time and degrees of sterilization F_0, by systematically adjusting the aforementioned parameters during the course of routine experimentation so as to obtain a desired degree of sterilization F_0, while minimizing the degree of thermal degradation of said heat sensitive composition due to extended durations of exposure to elevated temperatures. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

Furthermore, although none of the aforementioned references explicitly teach each of the instantly claimed elevated temperatures, durations of time and degrees of sterilization F_0, the Aikus '894 patent teaches a method of sterilizing a pharmaceutical composition comprising a heat sensitive compound by heating said composition to an elevated temperature for a short period of time, while the Grote '353 patent teaches limiting the duration of heat exposure of a heat sensitive compound, namely 3-(aminomethyl)-5-methylhexanoic acid (which is structurally similar to gabapentin), so as to minimize undesired decomposition and lactamization of 3-(aminomethyl)-5-methylhexanoic acid to the corresponding lactam, as discussed hereinabove. Therefore, it would have been prima facie obvious to modify the sterilization of said pharmaceutical composition comprising a heat sensitive gabapentin compound, as taught in the Carter '881 publication, to obtain a desired degree of

sterilization while minimizing undesired decomposition and lactamization, as suggested by the Aikus '894 patent and the Grote '353 patent. One of ordinary skill in the art would have been motivated, as well as had a reasonable expectation of success, to heat sterilize the pharmaceutical composition comprising a heat sensitive gabapentin compound by limiting the duration of heat exposure of said heat sensitive compound, so as to obtain a desired degree of heat sterilization while minimizing undesired thermal degradation and lactamization of said heat sensitive compound, as suggested by the Aikus '894 patent and the Grote '353 patent.

Conclusion

Claims 1-38 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David P. Stitzel, Esq. whose telephone number is 571-272-8508. The examiner can normally be reached on Monday-Friday, from 7:30AM-6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached at 571-272-0629. The central fax number for the USPTO is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published patent applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished patent applications is only available through Private PAIR. For more information about the PAIR system, please see http://pair-direct.uspto.gov. Should you have questions about acquiring access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David P. Stitzel, Esq.

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER